THE STRUCTURE AND PROPERTIES OF SOME SUBSTITUTED TETRAHYDROPYRIDINES

BY

JANET BROOKS PETERSON

B.S., University of Michigan, 1945
A.M., University of Illinois, 1948

AN ABSTRACT OF A THESIS

SUBMITTED IN PARTIAL FULFILLMENT OF THE REQUIREMENTS
FOR THE DEGREE OF DOCTOR OF PHILOSOPHY IN CHEMISTRY
IN THE GRADUATE COLLEGE OF THE
UNIVERSITY OF ILLINOIS, 1951

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Introduction

The structures of the trimers of 2,3,4,5-tetrahydropyridine itself have been clarified only recently.[1] It was of interest to attempt the preparation of several substituted Δ^1-tetrahydropyridines using the specific conditions under which the trimers of 2,3,4,5-tetrahydropyridine are formed, and to determine the effect of the substituents on the expected trimerization. Certain of the substituted trimers, if obtained, might serve as precursors of substituted 2,3′-bipyridines, otherwise difficult to prepare.

1-Alkyl-1,4,5,6-tetrahydro-2-picolines undergo a rather unusual rearrangement, the so-called Lipp rearrangement, upon treatment with aliphatic aldehydes.[2] The products of this reaction are 1-alkyl-3-acetylpiperidines, also possible intermediates in the preparation of substituted pyridines. A second object, then, was to extend the study of this reaction, first to 2-substituted Δ^2-tetrahydropyridines with an unsubstituted nitrogen atom.

Discussion of Results

When 1-chloropiperidine, prepared by the action of a chlorinated lime solution on piperidine acetate, is treated with ethanolic potassium hydroxide, 2,3,4,5-tetrahydropyridine is not obtained as such but in the form of its solid, structurally isomeric trimers, α-tripiperideine and isotripiperideine.[1] Usually both of these substances are isolated. α-Tripiperideine is readily isomerized to isotripiperideine in about 60% yield by refluxing in acetone with a catalytic amount of piperidine hydrochloride. In the present work, isotripiperideine was dehydrogenated directly to 2,3′-bipyridine (2-5% yield) and pyridine by heating with palladium-on-asbestos at 300°. The products were identified by comparison of their picrates

with authentic samples.

The products of the reaction between the 1-chloropipecolines, prepared in the same way as 1-chloropiperidine, and ethanolic potassium hydroxide depend upon the position of the methyl group.

The reaction of 1-chloro-2-pipecoline with ethanolic potassium hydroxide gave 1,4,5,6-tetrahydro-2-picoline, as the sole product isolated, in 30-50% yields (based on 2-pipecoline). The probable intermediate, 3,4,5,6-tetrahydro-2-picoline, is stabilized by rearrangement to the relatively stable monomeric 2-substituted Δ^2-tetrahydropyridine rather than by trimerization since the 2-methyl group undoubtedly hinders the latter reaction.

An extension of the Lipp reaction to 1,4,5,6-tetrahydro-2-picoline and acetaldehyde did not yield the expected 3-acetyl-2-pipecoline. An unstable product, $C_8H_{13}N$, was isolated which is probably 3-ethylidine-3,4,5,6-tetrahydro-2-picoline. Support for this structure is found in infrared data and in the low-pressure hydrogenation of the compound to $C_8H_{17}N$. The latter substance is indicated to be 3-ethyl-2-pipecoline since it is a secondary amine and it is not 2-*n*-propylpiperidine. The compound, $C_8H_{13}N$, was not dehydrogenated at 160-175° with palladium-on-asbestos. Heating at 275-300° in a sealed tube with palladium-on-asbestos gave a mixture of products none of which could be positively identified.

Treatment of 1-chloro-3-pipecoline with ethanolic potassium hydroxide gave only a viscous syrup which could not be crystallized. It was probably a mixture of structurally isomeric trimers produced by the trimerization of the two possible intermediates, 3,4,5,6-tetrahydro-3-picoline and 2,3,4,5-tetrahydro-3-picoline.

The action of ethanolic potassium hydroxide on 1-chloro-4-pipecoline gave a single, crystalline product in 26% yield (based on 4-pipecoline). From its composition and its infrared absorption spectrum which showed no absorption in the

region characteristic of NH groups, it was concluded that the substance must be 4,4′,4″-trimethyl-α-tripiperideine. Isomerization of this compound to the homologous isotripiperideine did not go in the expected manner. Hydrogenation of the non-crystalline product of the attempted isomerization gave a substantial amount of 4-pipecoline, the only product positively identified. Dehydrogenation of the isomerization product gave a low yield of 4-picoline, the only product isolated.

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VITA

The author was born in New York City on March 15, 1924. She attended the public schools in and near that city and graduated from Bronxville High School, Bronxville, New York, in June, 1941. In September of the same year she entered the University of Michigan and received the Bachelor of Science degree from that institution in June, 1945. From August, 1945 to July, 1946, she was employed as a research assistant at The Johns Hopkins University. In September, 1946 she enrolled in the Graduate College of the University of Illinois and in February, 1948 received the degree of Master of Arts. She held part-time teaching assistantships from September, 1946 to June, 1947 and from September, 1948 to June, 1949 and a University Fellowship from September, 1949 to June, 1950.

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